Health Economics Common Fund Diffusion of Medical Technology Workshop

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Acronym Definitions

Acronym	Definition
ACTION	Accelerating Change and Transformation in Organizations and Networks
AHRQ	Agency for Healthcare Research and Quality
BD2K	Big Data to Knowledge
BMS	bare metal stent
CAS	carotid artery stenting
CDOM	Center for Delivery, Organization, and Markets (AHRQ)
CEA	carotid endarterectomy
CEPI	Center for Evidence and Practice Improvement (AHRQ)
CHD	coronary heart disease
CHF	congestive heart failure
CMS	Centers for Medicare and Medicaid Services
CVD	cardiovascular disease
DES	drug-eluting stents
EU	European Union
FDA	Food and Drug Administration
FFS	fee-for-service
HCCI	Health Care Cost Institute
HCS	Health Care Systems (NIH)
HCOS	Healthcare Organization Services
HCUP	Healthcare Cost and Utilization Project
HRR	Hospital Referral Region
ICD	implantable cardioverter defibrillator
IMRT	Intensity-Modulated Radiation Therapy
MHOS	Medicare Health Outcomes Survey
MI	myocardial infarction
NCHS	National Center for Health Statistics
NCI	National Cancer Institute
NIH	National Institutes of Health

NIMH	National Institute of Mental Health
OECD	Organisation for Economic Co-operation and Development
PAR	Program Announcement Reviewed by the Institute
PCI	percutaneous coronary interventions
PCORI	Patient-Centered Outcomes Research Institute
RCT	randomized control trial
RFA	Request for Applications
SBRT	Stereotactic Body Radiation Therapy
SEER	Surveillance, Epidemiology, and End Results Program
TAVR	transcatheter aortic valve replacement

Meeting Summary

Introduction

The Steering Committee for the cooperative agreements funded by the National Institutes of Health (NIH) Health Economics Common Fund Program in response to *Diffusion of Medical Technology and Effects on Outcomes and Expenditures* (RFA-RM-12-023) convened a workshop on May 5 and 6, 2016, to share progress and to discuss case studies on health care technology diffusion, innovation, physician networks, and characteristics associated with diffusion. The workshop included researcher presentations as well as presentations by representatives of the National Cancer Institute (NCI), Centers for Medicare and Medicaid Services (CMS), and the Agency for Healthcare Research and Quality (AHRQ). The field of health care technology diffusion cuts across many disciplines, which is reflected in the diverse areas of study represented. Participants engaged in discussions on the topics of cross-national comparisons, diffusion, and health disparities, and resources needed in order to realize progress in the field. This document summarizes the workshop proceedings. The workshop agenda and a list of participants are included as Appendices 1 and 2, respectively.

Challenges and Opportunities

The field of health care technology diffusion is broad and involves research at multiple levels of analysis, including hospitals, providers, and patients. Participants discussed barriers that hinder the advancement of the field and noted how often these barriers center on data access and availability. The CMS data are a valuable resource, but the 20 percent sample was too small for fine-grained analysis of diffusion of individual drugs, so many analysts will need access to the full set of claims data, which can present barriers. Participants expressed concern that access to data has become increasingly difficult. Basic information including state identifiers has been removed from many datasets including those from CMS and the National Center for Health Statistics (NCHS). The Surveillance, Epidemiology, and End Results (SEER) Program-Medicare Linked Database contains data on fee-for-service (FFS) beneficiaries, but that portion of the population is decreasing. In the future, these data will be less representative of the general population. Merging data on FFS beneficiaries with other datasets would be beneficial to researchers. The SEER-Medicare Health Outcomes Survey (MHOS) Linked Data Resource includes data on Medicare Advantage enrollees. However, the SEER-Medicare Linked Database and the SEER-MHOS dataset are not linked.

The field is moving beyond CMS claims data towards Big Data. The IMS Health files, for example, can be used to characterize organizational structures in a dynamic way. It is a challenge for independent investigators who are not connected to a large institutional infrastructure to use these data because of the costs associated with purchasing access to larger databases such as that of the IMS Healthcare Organization Services (HCOS). The field would be better served if data access were more affordable to independent investigators.

There are big start-up costs for using both public and private databases such as Optum, Health Care Cost Institute (HCCI), and the CMS. Purchasing access to data on 30 million individuals for

social network analysis, for example, is extremely expensive because some database warehouses charge on a per patient basis. The CMS currently negotiates data access agreements with individual investigators and NIH Institutes. Participants discussed the potential benefit of negotiating data access at the NIH level, rather than at the individual investigator level.

Collaborating with other NIH initiatives might also push the field of diffusion forward. NIH's Big Data to Knowledge (BD2K) initiative or the NIH Health Care Systems (HCS) Research Collaboratory might offer valuable resources. BD2K is working toward the ambitious goal of making biomedical data findable, accessible, interoperable, and reusable (FAIR), which will increase the value of the data and make it easier to locate. One of the goals of the HCS Research Collaboratory is to partner with health care systems in the conduct of pragmatic clinical trials and availing of electronic health data. Hypotheses within different health care systems or within health insurance companies that could move the field forward on a broader scale could potentially be tested. AHRQ also has produced data resources that could be useful to researchers working on diffusion.

Participants expressed interest in using diffusion research to investigate health disparities. Disparity enhancing and disparity reducing diffusion models are ways in which the relationship of diffusion and health disparities might be conceptualized.

Cross-national studies can be valuable, particularly in the case of medical devices, because they tend to diffuse more quickly in the European Union (EU) than in the United States, which has more stringent Food and Drug Administration (FDA) regulations. The Wennberg International Collaborative group and the Organisation for Economic Co-operation and Development (OECD) are two entities that might facilitate cross-national investigations.

Linking an extremely rich data set with one that has more limited information is potentially beneficial but can be a challenge. Developing and sharing statistical methods to address this problem would be very helpful as it is an issue that many researchers face.

Participants expressed interest in a website or listserv as a potential tool in which diffusion researchers could share data. The existing Dartmouth website (www.dartmouthdiffusion.org) might be a platform for researchers to share data, code, and ideas.

Health Economics Program Cooperative Agreements

Technology Diffusion Pathways

Haiden Huskamp and Sharon-Lise Normand, Harvard University

This study is using Medicare enrollment and claims data, clinical registry data from the state of Massachusetts, IMS Health HCOS data on organizational affiliations for physicians, the American Medical Association Physician Masterfile, and commercial claims data to identify organizational characteristics associated with the diffusion of new technologies, use of lower and higher value services, and spending for new technologies and for lower versus higher value

services. Current analyses are focused on bevacizumab, drug-eluting stents (DES), modeling correlation among diffusion curves, second generation antipsychotic medications, and low-value services.

Bevacizumab is a high-cost, targeted therapy with minimal survival benefit for most cancers; these characteristics make it an ideal candidate for diffusion research. One goal of this study is to assess the diffusion among oncology practices for all cancers and by cancer type, practice size, and academic affiliation. Another goal is to look at between-practice variation and how this variation might be explained by different features of those practices, cancer type, and approved versus non-approved indication. The diffusion curves showing respectively time to first use and time to 10 percent use of Bevacizumab were most rapid for colorectal cancer, likely because it was the first type of cancer for which the drug was approved in 2004. Different relationships were visible based on how use was characterized. Results indicate that large provider practices adopted the therapy faster than small practices. Academic practices had higher rates of diffusion to first time use but slower time to 10 percent of patients getting therapy. Variation in diffusion rates was observed between oncology practices. A patient from a practice that was one standard deviation above the mean was two and a half times more likely to have an infusion with Bevacizumab than practices one standard deviation below the mean.

DESs for coronary syndromes diffused quickly when first introduced in 2003, but then in 2006 concern emerged about delayed adverse events including thrombosis. This research assessed the factors that predict adoption and whether these same factors also predict de-adoption. The hospital rates of DES use were compared with the use of bare metal stents (BMS) as a function of hospital and patient characteristics. Results of the analysis indicate a rapid rate of diffusion of DES to almost 90 percent of all patients versus BMS. In 2006 there was a sharp drop in DES use, which was attributed to stent thrombosis complication reports. Geographic variation was evident in the rate of adoption and de-adoption of these two types of stents. Diffusion of DES as compared with BMS was faster in Massachusetts than in the rest of the country the first year, but de-adoption was also faster. Next steps include an analysis of hospital characteristics and how they are associated with diffusion rates.

The methodological work of this project will identify the underlying features driving new medical technology adoption for medical practices. The goal is the identification of characteristics of oncology practices and physicians that are associated with the adoption of new drugs. Modeling data from all practices and all technologies simultaneously is computationally challenging. Each organization has multiple diffusion curves. Investigators will analyze which organizational characteristics are associated with diffusion. Future studies will investigate the diffusion of second generation antipsychotic medications. These drugs were highly anticipated since it appeared that they had attenuated side effects. Within a few years it became apparent that they had their own risks including metabolic syndrome and cardiovascular disease (CVD). Questions to be addressed include whether certain types of organizations adapt and use lower risk drugs more rapidly than other organizations. Patient and provider characteristics will be examined to determine whether these are associated with

second generation drug use. Future research also will characterize the use and spending on low-value services overall and by medical practice.

Empirical Studies of the Development and Diffusion of Medical Technologies

Heidi Williams, Massachusetts Institute of Technology

The goal of this project is to empirically investigate how patents shape the development and diffusion of medical innovations. New data and empirical methods are necessary to address the extent to which patents provide incentives for the development of new technologies and whether they hinder subsequent innovation. The more effective patents are in inducing research investments in new technologies, the stronger the case for longer or broader patents. On the other hand, the high cost of patents may hinder subsequent innovation. Evaluating the costs and benefits of patents is important for optimal design.

One aspect of this study is to investigate whether the granting of a gene patent is associated with subsequent innovation as compared to genes that did not receive a patent. Williams created a database of gene patent applications filed with the U.S. Patent and Trademark Office, linked to information on which applications were granted patents. Follow-on innovation was measured by determining the use of the patented and non-patented gene in subsequent scientific publications, clinical trials, and gene-based diagnostic tests. Data on rejected patent applications are not available prior to 2001, so the study focuses on data from 2001 and later. Scientific publications were examined both before and after patent applications for genes were filed starting in 2001. Publications linked to genes included in accepted and rejected patent applications were compared. Consistent with accepted and rejected applications being a reasonable comparison, publications on the two groups of genes were similar prior to 2001. Consistent with gene patents having little effect on subsequent innovation, publications on the two groups of genes were also similar after 2001. The clinical trials data show similar trends.

An alternative source of variation in Williams' study leverages variation in leniency across patent examiners as a determinant of why some patent applications are granted and others are rejected. The assumption underlying this approach is that patent applications are quasi-randomly assigned to patent examiners upon submission to the U.S. Patent and Trademark Office. Preliminary evidence suggests that the likelihood of patent approval is indeed associated with the leniency of the assigned examiner. Future research will empirically evaluate the assumption of quasi-random assignment and will implement this analysis in the universe of all patent applications, including non-human gene applications. Ongoing work is focused on exploring heterogeneity in the estimated treatment effects and strategies to make the results of this work more useful for other researchers.

Technology Diffusion, Health Outcomes, and Expenditures

Jonathan Skinner, Dartmouth College

This study investigates the intriguing question of why certain physician practices, hospitals, or regions diffuse new technologies rapidly versus slowly. Three categories of health care innovations are explored: (1) innovations that are cost-effective for nearly every patient, such

as A1c testing for diabetics; (2) innovations that have heterogeneous benefits (cost-effective for some, cost-ineffective for others) and that might diffuse rapidly in patients that were not tested in a randomized trial; and (3) innovations with uncertain or low benefits.

The diffusion of medical technology has a major impact on patient outcomes and health care resource utilization. As part of this cooperative agreement, the Dartmouth Institute for Health Policy and Clinical Practice created the first publicly available source providing researchers, payers, regulators, and innovators with metrics quantifying the temporal and regional patterns of diffusion of medical interventions. This is a readily available online platform offering interactive tools that can aid in the understanding of innovation across a spectrum of new and established treatments. The website (www.dartmouthdiffusion.org) enables the user to use interactive tools to apply diffusion metrics and download longitudinal data from the Dartmouth Atlas. Currently, surgical procedure data are available for download in CSV, Excel, SAS, and Stata formats. Data are available for different years and at the geographic level. Future goals are to improve the time series patterns by region and by county in terms of utilization rates.

Asking why new technologies are slow to diffuse is a conventional question; a less conventional question is why new technologies diffuse so quickly. The investigators developed a Bayesian model of technology diffusion and tested it using a registry of implantable cardioverter defibrillators (ICDs) and Medicare claims data. The outcomes of rapidly diffusing regions were compared with slowly diffusing regions. The expectation was that rapidly diffusing regions would have better outcomes and greater adherence to the guidelines of use. The risks for individuals with congestive heart failure (CHF) include sudden myocardial infarction (MI) and progressive heart failure in which people progress through Classes I-IV of the New York Heart Association stages of disease. The guidelines for whether a patient should receive an implantable device include those with Class II or III CHF (Class I patients are not sick enough and Class IV are too sick and patients must be diagnosed with CHF for at least 3 months). Results indicate that diffusion rates jumped in 2006 when ICDs were approved for preventative use. Prior to 2006 they were used only for MI patients. Diffusion rates showed regional variation patterns on a national level. In 2010, Medicaid investigated some of the hospitals with rates of patients receiving defibrillators higher than prescribed by guidelines, a characteristic of areas with high rates of diffusion. One implication of the model is that overconfident agents will diffuse more rapidly with potentially adverse effects on outcomes.

In a test of the overconfidence hypothesis, patients of rapid adopters did not have significantly better clinical outcomes. Several cities had both high ICD diffusion rates and high mortality rates. Possible reasons for the high diffusion rate in these cases include overconfidence and financial motivations. In this example, the most skilled physicians were not necessarily the ones leading the way in rapid adoption of a new technology. The frequency of Hospital Referral Region (HRR)-level mortality for ICDs from 2006-2013 was substantially below the mortality rate found in randomized control trials (RCTs), which is consistent with other research. For example, mortality in the non-trial Medicare population following carotid endarterectomy was

substantially higher than the mortality rates found in the RCTs that demonstrated efficacy of the procedure.[1]

The results of these analyses have several implications. Highly skilled and knowledgeable innovators are not the most rapid adopters of ICDs. On average, the net value of ICDs are substantially below that promised by RCTs. Learning-by-doing exists but only for diagnostic ability, not skills.

Diffusion Case Studies

Factors Associated with Adoption or Abandonment of Surgical Procedures

Philip Goodney, Dartmouth College

Exnovation is the process by which established medical practices are abandoned. An influential meta-analysis of the diffusion of technology has been cited more than 4,000 times and includes a review of hundreds of papers in the field.[2] Only one of the articles focused on exnovation. Information about how medical innovations enter clinical care exists, but there is less information on how such innovations are dropped or abandoned. Goodney used carotid atherosclerosis to illustrate the concept of exnovation. His work also is exploring differences in physician characteristics and their use of carotid revascularization over time.

Carotid artery disease occurs when there is plaque buildup in the carotid artery, which, if left untreated, may result in a stroke. This plaque can be removed via a carotid endarterectomy (CEA) or a carotid artery stenting (CAS) procedure. CEA procedure rates are influenced by many factors. The outcomes from this procedure have not always been favorable and therefore, rates decreased over time. Subsequently, evidence from some RCTs as well as improvements in the procedure led to an increase in rates. Some substitution effects were observed as fewer CEA were conducted and the use of CAS increased.

Goodney and colleagues are creating linked datasets using Medicare claims data, Vascular Quality Initiative, and Doximity to explore physician- and practice-level factors associated with exnovation. Preliminary analyses indicate that surgical rates of carotid revascularizations in the under and over age 80 groups declined at similar rates. The decline in CEA does not appear to be explained by a reduction in the rate of procedure in asymptomatic patients, which suggests that exnovation is not happening based on age or symptom status. Goodney explored associations of patient characteristics and physician- and practice-level factors with exnovation. Results indicate that the patients receiving carotid revascularizations were similar across the different physician specialties that perform these procedures; however, there was large variation by physician specialty. Rates of CEA among general, cardiac, and thoracic surgeons

[1] Wennberg, T., Lucas, F. L., Birkmeyer, J. D., Bredenberg, C.E., & Fisher, E.S. (1998). Variation in carotid endarterectomy mortality in the Medicare population. *JAMA, 279*, 1278-1281.

[2] Greenhalgh, T., Robert, G., Macfarlane, F., Bate, P., & Kyriakidou, O. (2004). Diffusion of innovations in service organizations: Systematic review and recommendations. *Milbank Quarterly, 82*, 581-629.

have declined over a 10-year time frame. Vascular surgeons, however, showed no decline in the rate these procedures are performed.

The characteristics of physician exnovators were examined. Exnovators were more experienced, participated in clinical trials, practiced in larger physician groups, and were less likely to be vascular surgeons. Specialties with a larger practice share of carotid revascularization procedures at baseline were less likely to abandon the procedure as aggressively. This analysis of exnovation, using a surgical procedure as an example, has significant similarities to accepted models of diffusion. Future work will focus on an analysis of referral and practice patterns and associations with exnovation. The complex dynamics within and among physician networks and rates of exnovation also will be examined.

The Exnovation of Potentially Hazardous Medical Care: State Prescribing Regulations and Prescription Opioid Use

Ellen Meara, Dartmouth College

There has been a dramatic increase in prescription opioid sales and deaths since the 1990s, with a leveling off only in the last 5 years. Prescription opioids are highly addictive. In response, states have implemented various restrictions on the prescribing and dispensing of controlled substances, targeting the prescribers, the dispensers, and the patients, including prescription limits, prescription drug monitoring programs, tamper-resistant prescriptions, pharmacist and physician exams, identification requirements, doctor shopping, and pain clinic regulations. These laws have been heavily promoted by the Centers for Disease Control and Prevention and other organizations, but little evidence exists as to their effectiveness. The regulations are costly to implement and add burden to the physicians, patients, and dispensing facilities. Meara's work investigates whether such state-level restrictions reduce potentially hazardous opioid prescribing and non-fatal overdose.

Meara and colleagues focused on disabled Medicare beneficiaries because this population has 10 times the rate of overdose deaths than the total U.S. population. It is estimated that disabled Medicare beneficiaries represent about one in four prescription opioid overdose deaths. The study population included one million observations per year for a total of almost nine million observations (40 percent of Medicare part D users). The outcomes included any user of opioids (almost half of the study population), chronic users (prescription filled every calendar quarter), four or more opioid prescribers (highly associated with overdose), daily morphine, and one or more non-fatal prescription overdoses. Each outcome was predicted as a function of each of the individual laws controlling for state effects and several other factors, including the existence of medical marijuana laws and legislative intensity. Preliminary results indicate that the non-fatal opioid overdoses are not associated with any individual law. Intensity of legislation was not associated with chronic opioid use.

Despite widespread adoption of opioid restrictions, there is no evidence that use, potentially hazardous prescribing, or non-fatal overdose are affected by the laws. In other words—these

restrictions do not facilitate exnovation. These results suggest that states need to refine existing laws and pursue other strategies for regulating opioid use.

Choice of Treatment for Prostate Cancer

Bruce Jacobs, University of Pittsburgh

Prostate cancer is the most common cancer for men in the United States, affecting about one in seven men. It also is very expensive to treat—$13 billion was spent on treatment and care of prostate cancer patients in 2010. It is possible that one driver of the costs of prostate cancer is the diffusion of expensive new technology and treatments for the disease. The Da Vinci Robotic Surgery for prostate cancer was introduced in 2000; Intensity-Modulated Radiation Therapy (IMRT), a radiation treatment for prostate cancer, was introduced in 2001; and in 2007, Stereotactic Body Radiation Therapy (SBRT) was introduced.

Jacobs analyzed the adoption trends of certain prostate cancer treatments and factors that might be influencing the adoption rates. Trends in the 2000s indicate a drastic increase in robotic procedures and decrease in the standard open approach. The rapid adoption of the robotic technology would lead one to believe that the evidence with regard to improved outcomes is robust, particularly because this technology comes at a higher cost. A review of the evidence does not suggest that one procedure is superior to the other in terms of outcomes.

Jacobs analyzed adoption rates of two radiation treatments: IMRT and 3D conformal therapy. IMRT almost replaced 3D therapy from 2001 to 2007. This is another example of rapid diffusion of a costly therapy that is not supported by clinical evidence. Comparisons of adoption rates of IMRT and SBRT therapies showed that IMRT was adopted at a rapid rate over the first 5 years while SBRT was adopted more slowly. IMRT radiation is delivered in 40 treatments over an 8-week period and is more expensive than SBRT. SBRT requires less time and fewer treatments at a higher dose—five treatments total over less than 3 weeks. Clinical outcomes, such as 5-year recurrence-free survival, for the two treatments were the same and toxicity was similar. One factor that might be influencing different adoption rates is general overtreatment of prostate cancer in patients with low-risk disease, high risk of non-cancer mortality, or both.

The study involved interviews of oncologists treating prostate cancer about clinical effectiveness of radiation treatment options, barriers to adoption or exnovation, and the role of patient driven treatment requests. Some thought that there was not much difference in the therapies in the short run, although there was some concern about the long-term effects of the high-dose radiation. Decisions about whether or not to adopt new technology happens before 15 to 20 years of follow-up data are available. Participants noted that barriers to adoption include insurance coverage, lack of published effectiveness data, and reimbursement structures. For example, if reimbursement is provided per-visit, then practices administering the SBRT would receive fewer payments than those using IMRT.

Future research will include the identification of health systems with extreme rates of SBRT use (identified with SEER-Medicare data); market and sociodemographic factors associated with SBRT adoption among these networks; and interviewing associated radiation oncologists,

hospital leaders, payers, and policymakers. The goal is to identify targets for interventions to drive providers toward the highest value technologies.

General Discussion

Factors Influencing Diffusion

It is clear that clinical effectiveness is not necessarily the main driver of diffusion of new technologies. Participants discussed the possibility that the shift away from surgery to radiation in prostate cancer treatment is being driven by the different side effects, which are more favorable for radiation. It is possible that there are provider characteristics or preferences that influence diffusion and that some providers might be overly confident or greedy. These attributes should be investigated across technologies and within providers. The amount of training involved in the particular specialties and even the variation within training in general surgery is a broader characteristic that would be interesting to investigate.

Data Access and Methods

Access to data and data linkages can be a barrier to research on the diffusion of medical technology. Some states have cancer registries linked to Medicare; however, conducting analyses in a single state limits power and generalizability.

There are new methodological approaches for linking datasets that differ in the richness of data they contain. Common statistical methods could be useful across projects and research questions. Developing and testing these tools among the Steering Committee members to create a shared resource would be extremely beneficial to the research field. Several of the meeting participants agreed that novel, non-Bayesian methods need to be developed.

Care Coordination

Current health care policy promotes coordinated care. However, one unintended consequence of the Stark Law is that it could limit coordination and collaboration among physicians. Health economists could help delineate under what circumstances care coordination is detrimental or beneficial in promoting patient care. Meeting participants agreed that this was an important issue that warranted further investigation. So-called one-stop shopping for health care services might be convenient and beneficial for patients, but the potential for abuse should be investigated.

Guidelines of Care

Guidelines of care are another potentially interesting topic for further investigation. There is no gold standard for the optimal proportion of guideline-consistent care for a provider. For example, a provider that is 100 percent guideline-compliant for ICDs would not be considered effective. Clinical care is more nuanced than what is reflected in the guidelines. Normand had a similar challenge in her work with determining the time-to-10 percent adoption measure because it is not clear what the optimal number is. Determining the equilibrium position is appropriate for economists to address. Theoretical modeling might provide some guidance for situations in which this optimal percentage can be delineated.

The question of how diffusion of technology works between physicians within a practice was discussed as a potential future topic of analysis. Normand has been working on such questions with Nancy Keating, but their work is still in its preliminary stages.

Dissemination and Implementation Research at the NIH

David Chambers, National Cancer Institute

Chambers spoke about trans-NIH initiatives on dissemination and implementation research and encouraged researchers to start thinking about the different ways in which interventions and innovations make it into practice. He noted that a classic paper showed that it takes 17 years to turn 14 percent of original research to the benefit of patient care. Assuming perfect access, testing, and follow-up, a magic pill that effectively treats a specific illness might only result in a small benefit if only half of the insurers choose to cover it, half of the health systems choose to train clinicians to prescribe it, half of those trained clinicians choose to prescribe it, and half of those clinicians' patients get tested. The scientific community primarily focuses on efficacy and effectiveness, but the factors influencing dissemination and implementation of research are important dimensions that maximize the potential benefits of interventions.

Dissemination and implementation need to be addressed in a robust way. Dissemination research should provide more information on how the evidence is created, packaged, transmitted, received, and translated into action. Many early efforts to translate research into practice ignored these steps and assumed that all of this information was known. Each of the steps in the dissemination process should be subject to testing so that it can be improved. Implementation research should focus not only on what is delivered, but how, where, and under what circumstances it gets delivered in health care or community settings.

Chambers identified several areas ripe for exploration: sustainability of evidence-based practices in a changing context; adaptability/evolution of evidence-based practices over time; impact of dissemination strategies on practice; scaling up practices across health plans, systems, networks, and nations; and de-implementation/exnovation. A trans-NIH set of funding opportunity announcements led by the Implementation Science Team in the Division of Cancer Control and Population Sciences at NCI prioritizes the full range of dissemination and implementation research, including the following topics:[3]

1. Tailoring: Rather than saying there is a common or standard way in which measurement-based care should be implemented, context-sensitive and tailored ways of implementation should be investigated. It is possible that variations exist in how communications and systems operate in clinics, for example.

2. De-implementation (i.e., exnovation): How are already implemented interventions removed that have been deemed sub-optimal or ineffective? The Choosing Wisely

[3] Current funding opportunities can be found at http://cancercontrol.cancer.gov/IS/funding.html#methodhead.

initiative has been successful at identifying ineffective interventions that need to be replaced or removed.[4]

3. Scaling-Up Evidence Based Practices: Interventions are typically implemented in a relatively small number of clinics or communities. The DIAMOND project in Minnesota, for example, is a state-wide effort to scale up effective depression care using reimbursement strategies and practice facilitation.

Theories that depart from the idea of a linear pathway from research to practice and instead use a more iterative, reciprocal approach to learn at every stage may be beneficial to ensuring the use of research findings in health care settings. There is interest at NIH in a range of scientific questions for dissemination and implementation and the optimal designs to answer them. Some investigators funded to do dissemination and implementation research also are using existing datasets to try to understand how technologies are adopted or de-implemented.

Critical Perspectives on Racial and Ethnic Differences in Health in Late Life

John Haaga, National Institute on Aging

Information about health disparities is typically examined at one point in time and conclusions are made about one group having better access to care when compared to another group. Another approach is to examine disparities from a temporal perspective and make conclusions about how one group is 10 or 15 years ahead of this other group. Work by Skinner motivated the question that there are persistent geographic laggards, or areas that were always 10 to 15 years behind the frontier. Disparity enhancing technology diffusion is one model that has dominated the thinking in this field. Patients with access to providers in teaching hospitals are more likely to get superior care than those without access to such services, which would mean disadvantaged groups are always playing catch up.

Research Examples

Skinner and Amitabh Chandra conducted a state-level analysis on the percentage of acute MI patients treated with beta blockers at hospital discharge in 2004, which was published as a chapter in a report of the Committee on Population at the National Academy of Sciences.[5] Their analysis showed that states with a higher average proportion of African Americans had adopted beta blocker use more slowly than comparison states.

Medical technology diffusion could also play a role in reducing health disparities. John Ayanian and colleagues investigated racial disparities in blood pressure, cholesterol, and blood sugar in Medicare Advantage patients using enrollment data and quality of care measures from the Healthcare Effectiveness Data and Information Set.[6] Blood pressure improved for both African American and Caucasian groups over a 5-year time period, but a gap still existed. This gap was

[4] Choosing Wisely is an American Board of Internal Medicine Foundation initiative. http://www.choosingwisely.org/

[5] See Chapter 16 of the report at http://www.nap.edu/read/11086/chapter/1.

[6] Ayanian, J. Z., Landon, B. E., Newhouse, J. P., & Zaslavsky, A. M. (2014). Racial and ethnic disparities among enrollees in Medicare Advantage plans. *New England Journal of Medicine, 371*, 2288-2297.

evident in all areas of the country except in the West—in which health care coverage and services are dominated by Kaiser Permanente—where a disparity was not found. Further study is needed, but it appears that an electronically based communication intervention between Kaiser and its beneficiaries could explain the absence of racial disparity in outcome.

A final example is a study of diverging trends in all-cause mortality among those 50 and older.[7] In the mid-1960s, the worst states for mortality at older ages were scattered around the United States (e.g., several New England states, North Dakota). By 2013, the divergence had grown and poor health was much more clustered in areas such as the Mississippi Delta, southern and central Appalachia, Arkansas, and Oklahoma. The other states experienced a decline in mortality similar to the pattern seen in European countries. This pattern can be replicated in various levels of analysis including counties and county groups. Ever since about 1960, almost all the improvement in treatments has been for heart disease, stroke, and injuries. Therefore, explanations for big changes and big disparities in this period can be found by looking for factors affecting CVD, stroke, and diabetes.

For whites in the Baby Boom cohorts, there has even been an increase in mortality rates, especially pronounced in rural areas.[8] The causes of that trend might be quite different from lagging diffusion of effective medical care. The broader perspective is one of declining mortality and improving health for most Americans for most of the time since the mid-20th century—what demands explanation is why the improvement was so slow in the United States compared to other rich and even middle-income countries and why it was especially slow in some parts of the country. Lags and unevenness in diffusion of effective new technology and incomplete replacement of ineffective technology might help explain persistent disparities.

Discussion: Do Diffusion Studies Explain Disparities?

Health disparities can be the result of multiple factors, including medical technology diffusion. Participants offered examples of studies demonstrating various features of disparities and the role that technology diffusion might play.

Karaca-Mandic is currently investigating health disparities and patterns of de-adoption of medication for which safety evidence argues against their use. She hypothesizes that disparities are driven by the delivery side and that certain minority groups are disproportionally over-treated with such medications in lower resourced areas. Organizations might be creating a resource barrier that contributes to the persistent disparities.

Normand collaborated with a psychiatrist to conduct a longitudinal study using state Medicaid data to examine disparities in diffusion of a novel treatment for schizophrenia. Relative to whites, quality of care was lower for blacks in every state and also lower for Latinos except in

[7] Fenelon, A. (2013). Geographic divergence in mortality in the United States. *Population and Development Review, 39*, 611-634.

[8] Case, A., & Deaton, A. (2015). Rising morbidity and mortality in midlife among white non-Hispanic Americans in the 21st century. *PNAS, 112*, 15078-15083.
Snyder, S. E. (2016). Urban and rural divergence in mortality trends: A comment on Case and Deaton. *PNAS, 113*, E815.

North Carolina. Within each state, counties differed in quality and disparities. Normand could not find any county level infrastructure or other county level characteristics to help explain those gaps.

Meara and her collaborators looked at different causes of infant death in the 1970s and 1980s. As death rates decreased, health disparities increased. They determined that the rates decreased in causes of infant deaths in which more research was being conducted. The increase in racial disparities observed was concluded to be almost entirely due to surfactant treatment for respiratory distress syndrome, which is a breathing disorder that white infants suffer from at a greater rate than black infants. For babies of the same weight, black infants had much healthier lungs. While this research had a tremendous effect on population health, it actually exacerbated the disparity.

Janet Currie recently published a National Bureau of Economic Research working paper on mortality trends for people over and under age 50. Her results indicated that among adults age 50 and over, mortality declined more quickly in richer areas than in poorer ones, resulting in increased inequality in mortality. She found a narrowing of income differentials, education differentials, and black/white differentials among younger age groups. These results are interesting because the differences in trends are age dependent.

Skinner noted that patients served in an area where the doctors are not diffusing an effective treatment are all unfortunate whether they are African American or Caucasian. African Americans tend to go to disproportionately higher mortality hospitals (e.g., the disparity exists at the hospital level, not the physician level). Targeting several poor quality hospitals that serve majority minority populations could greatly reduce disparities.

Agha provided an example from her work on pulmonary embolism. She reported that African American patients were less likely to be tested even though they are at increased risk of pulmonary embolism, indicating a within-physician disparity. These results demonstrate the importance of not making generalizations from one disease to others.

Partha Bhattacharya noted that the representativeness in RCT populations is important for findings of disparities. Early adoption also may come with possible risks. A patient that had a DES placed in the early 2000s had an increased risk of stroke, for example. If there was a racial disparity in that procedure, the slow adopters might be spared (thalidomide is another example).

Rare diseases are less likely to be studied. Disease prevalence is weighted based on the majority population, not based on disease prevalence in minorities. Because of the differences in general population versus minority population disease prevalence, public and private investments in research will exacerbate health disparities.

Health disparities could be influenced by patients sorting to different providers. Another explanation is that patients go to the same providers, but the providers are making different choices for the same patients.

Innovation

Regulating Innovation with Uncertain Quality: Information, Access, and Risk in Medical Devices

Robert Town, University of Pennsylvania

The quality of newly developed products is often uncertain and regulators must decide how much testing to do before launch. More testing means more information and less risk to consumers but it also means less access because of later entry to market and/or greater entry costs. Medical devices are a $150 billion industry in the United States. Data on market information, patient risk, and device quality and exogenous variation in regulatory policy are needed to analyze this issue.

Differences between EU and U.S. testing regulations and the approval process can be leveraged to address this question. The 1976 Medical Device Act categorizes devices into Class I, II, and III, with Class III considered a high risk group requiring an RCT. The FDA has both safety and efficacy standards whereas the EU employs only a safety standard, which can be met with limited clinical trials at lower cost. These regulation differences generally lead companies that enter both markets to enter the EU first while undergoing safety and efficacy trials in the United States.

Town used product level data for coronary stents to compare diffusion in the EU and U.S. markets and test a theory of regulation with uncertainty and learning to determine how much testing should be done before the launch of the device. The length of the clinical trial determines the amount of information that is available in the marketplace and that, in turn, determines which products will be introduced into the market based on marketability. It is expected that newer products will have a higher variance in utilization because people have different information and the variance of that information will be larger and more uncertain. It is also expected that products with more uncertainty will be used less. Regulatory differences do not appear to be driven by differences in disease or treatment. To determine whether this is learning by clinical trials, diffusion, or selection, Town looked at the same products that entered in the United States and found a similar pattern emerges.

Town estimated parameters of a demand system and used these parameters to determine the value of information and the optimal amount of information to be provided to the market. His analysis shows that the optimal length of a clinical trial is between 9 and 16 months, which is equivalent to the average trial length in the United States. The EU has 3-month clinical trials, but they get the benefit of spill-over information. If post market learning could be introduced, the clinical trial length could be reduced which could, in turn, lead to increases in welfare.

Town summarized by noting that there is a lot that can be learned from quantity data about information and risk; U.S. polices are close to optimal for stents; regulation innovation has meaningful effects via market structure; imperfect information can shut down a market; and his model clarifies how optimal regulation depends on rates of learning (risk tolerance) and

technological change (preferences). Town's future research will include studying the effects on innovation intensity and types and public versus private certification incentives.

Promoting Novelty in Science

Jay Bhattacharya, Stanford University

In isolation, acts of genius will rarely move a scientific discipline forward. Every new scientific idea needs vetting by the research community to be successful. In vibrant fields, scientists test others' new ideas. Bhattacharya is working to identify the structures and correlates of scientific environments that promote the acceptance of novelty, including ages of scientific team members, openness of funders to try novel ideas, and the willingness of journals to publish papers with new ideas.

Bhattacharya completed a text analysis on more than 16 million publications from Medline to estimate the age of ideas, distinguish important new ideas, and determine how novel the ideas in a particular paper are. He hypothesized that early career scientists are more likely to try out new ideas. There are costs and benefits of age of the researcher. Older researchers have vested interests in old ideas and greater non-research demands on their time. On the other hand, older researchers have the security of tenure to pursue risky new research paths. Bhattacharya made a number of conclusions based on his analyses: younger biomedical researchers are more likely than older ones to try out newer ideas; younger researchers, paired together with mid-career senior authors, are the most likely to try out newer ideas; and larger scientific teams are more likely than smaller teams to try out newer ideas.

Bhattacharya and colleagues also analyzed the innovativeness of medical journals and found that top journals, as measured by impact factor, are the most open to papers that try out newer ideas. However, there is considerable variation.

These findings have important implications for NIH and other research funding organizations. The biomedical research field needs structures in place that encourage testing innovative ideas. A research agenda that identifies system properties that encourage scientific innovation could help. Future research will include exploring the role of NIH in encouraging innovation in science and measuring links between innovative ideas in biomedicine and medical practice.

Dormant Therapies

Benjamin Roin, Massachusetts Institute of Technology

Roin's recent research has focused on the untapped potential of unpatentable drugs.[9] There is a potentially significant gap in the patent protection available for new drugs for several reasons: (1) new drugs require clinical trials to reach the market; (2) firms usually need monopoly protection to fund clinical trials; (3) patentability depends on the novelty of the idea for the

[9] Roin, B. N. (2009). Unpatentable drugs and the standards of patentability, *Texas Law Review, 87*, 503-570. Budish, E., Roin, B. N., & Williams, H. (2015). Do firms underinvest in long-term research? Evidence from cancer clinical trials. *American Economic Review, 105*, 2044-2085.

drug, not the need for a clinical trial; (4) many potentially valuable new drugs are no longer patentable; and (5) therefore, the public is likely missing valuable new drugs made from compounds that do not meet the standards of patentabilty—dormant therapies. Roin presented information about the gap between the need for and availability of patent protection.

There are several barriers to pharmaceutical firms' investments in research and development. Clinical trial data are needed to obtain FDA approval and to support marketing. However, clinical trials are extremely expensive—approximately $2.6 billion is spent on research and development for each new FDA-approved drug. These investments are susceptible to free riding and there is rapid generic penetration, which lessens potential profits because pharmaceutical companies need time for the novel drug to be on the market to realize the return on their investment.

Current standards of patentability require a drug to be novel, non-obvious, useful, and non-existent in nature; the latter is a result of the U.S. Supreme Court ruling on *Myriad Genetics*. If any detail about a drug or the idea of a drug is disclosed, even if that drug has not yet been developed for medical use, it is no longer novel and therefore cannot be patented.

The current standards of patentability have implications for bringing drugs to market that could benefit patients. For example, potentially beneficial dormant therapies that are unpatentable due to early disclosure might never be tested in a clinical trial because of an inability to find a commercial partner willing to develop the intervention without a patent. Pharmaceutical companies regularly screen drugs with non-novel compounds out of the development pipeline. In addition, the U.S. Patent and Trademark Office rejects numerous patent applications for drugs to treat a variety of diseases, such as HIV, cancer, diabetes, stroke, hypertension, cholesterol, and tuberculosis.

Roin proposed regulatory exclusivity as a potential solution to the problem. Clinical trials are needed to develop new drugs and firms need patents in order to fund those trials. However, patents are not always available for untested new drugs due to the current standards of patentability. Guaranteeing a sufficient exclusivity period for new drugs in exchange for successfully completing clinical trials is a potential solution.

The Pharmaprojects database is a valuable tool for examining outcomes. The group discussed what entities might be interested in supporting research to test the most promising unpatentable drugs.

Medicare Coverage and Evidence Development

Joseph Chin, Centers for Medicare and Medicaid Services

Researchers are often interested in understanding how Medicare coverage determinations are made. Statutory constraints limit the coverage decision process. The Social Security Act of 1965 authorized Medicare to pay for items and services reasonable and necessary for the diagnosis or treatment of illness or injury. The same approach is used with new services and technologies.

Medicare uses an evidence-based framework to determine coverage by assessing whether the evidence is sufficient to conclude that the item or service improves clinically meaningful health outcomes for beneficiaries.

CMS and the FDA have different statutory authority in regulating devices. CMS does not automatically cover devices, technologies, or lab tests that are FDA-approved. The FDA bases its decisions on safety and effectiveness. CMS coverage depends on whether the new device is reasonable and necessary for the diagnosis or treatment of illness or injury, whether there is an evidence base for clinically meaningful health outcomes, and for diagnostic, imaging, or laboratory tests, whether there is sufficient analytic validity, clinical validity, and clinical utility. CMS and the FDA review devices on different timelines. There is an FDA-CMS parallel review process being developed that shows promise. The FDA is looking for companies and technologies to enter into a pilot program. Manufacturers are encouraged to contact CMS early on when they are in discussions with the FDA to facilitate this collaboration. The manufacturer might be able to use the pilot study trial to satisfy requirements for both the FDA and CMS.

There is not much discussion between the CMS offices responsible for evaluating coverage and determining pricing. Costs are not considered in coverage determinations. Prices are derived based on a number of rules depending on whether the technology or innovation is a device or a drug. Many of the pricing formulas are driven by legislation. Pricing is often determined by reviewing prices on an existing diagnostic, genomic, or biomarker test that is similar to the one being considered.

Since 1999, CMS has tried to use very specific patient eligibility criteria to make coverage decisions. For example, coverage of a transcatheter aortic valve replacement (TAVR) is limited to a specific type of patient for whom evidence suggests clinically meaningful health outcomes. The same specificity is not observed for percutaneous coronary intervention (PCI) for stable angina. Services that have already been paid for are hard to amend. A device or drug that is covered broadly can be diffused to a population beyond that which was tested in the clinical trial. CMS does not have specific coverage decision guidelines for specific subgroups of patients. For example, trials for ICDs do not have older populations, but many ICDs are used for patients in their 80s and 90s. It is not known whether the ICDs are beneficial for people over a certain age, but it is difficult to restrict devices to certain age groups. Generalizability of results can also be a factor in coverage determinations.

Medicare and other insurers issue coverage rules but their ability to enforce the rules is limited. Providers have the power to limit use of a device or test. CMS uses contractors and recovery auditors to broadly scan documentation in medical records to ensure that the provider is adhering to CMS coverage guidelines and to spot cases of fraud and abuse. Restrictions are sometimes placed on the type of provider that can deliver a particular service. Carotid endarterectomies are conducted by both radiologists and vascular surgeons, for example. These decisions are made based on the available evidence and which providers are successful at doing which procedures.

The decision about whether a device or service is under a national coverage umbrella or under a local one depends on who is requesting it. A company will typically request a national determination for a new technology with insufficient evidence. There is no need for a national decision when the evidence is overwhelmingly positive and all insurers cover it. Requesting national coverage decision is often a last resort unless the request is covered in a clinical trial.

Discussion: What Can We Learn from Cross-national Comparisons

Leveraging cross-national differences in diffusion is a promising area of future research because considerable amount of heterogeneity can be observed. Not much is known about whether diffusion rates are too fast or too slow or whether diffusion reaches the right people. Payment models also vary across countries and, with cross-national data, could inform research on the consequences of different payment models. It is possible cross-national data could be obtained by working with a marketing firm that has a strong incentive to capture these data. Obtaining administrative data from various agencies and compiling them in a useful way is a challenge.

The United States is persistently worse than other countries in some health outcomes and diffusion may partially explain these differences. For example, the National Heart, Lung, and Blood Institute prematurely halted its Beta Blocker Heart Attack trial in 1981 after 26 percent lower mortality was experienced in the treatment group as compared to the control group.[10] By the mid-80s, Germany and France were using beta blockers universally. However, in the United States there was a 20-year delay before beta blockers were the standard of care. Contrary to expectations, the United States might be slow in adopting some technologies. By the time innovation reaches Arkansas, Australians have been using it in Perth for 20 years.

Innovations are often unveiled in Europe well before the United States. Primary PCI and TAVR are two such examples. It appears new technologies get an earlier start in Europe but then do not diffuse as rapidly into the population because of overall budget constraints. In contrast, new technologies have a slow start in the United States but then rapidly diffuse once Medicare issues a coverage determination.

Examples of Existing Resources

- McClellan, M. B., and Kessler, D. P. (2002). *Technological Change in Health Care: A Global Analysis of Heart Attack*. Ann Arbor, University of Michigan Press.
- the OECD health statistics website, which can be found at http://www.oecd.org/els/health-systems/health-data.htm.

Ongoing Related Projects

- Town presented data on stents being used in the EU, but not approved in the United States, which is an interesting way to study diffusion.
- Therese Stukel's current work involves cross-national comparisons between the United States and Canada.
- The Wennberg International Collaborative is analyzing data from different countries to study within-country regional variation, but diffusion has not yet been addressed.

[10] (1981). The beta blocker heart attack trial. *JAMA, 246*, 2073-2074.

- Normand is currently working on a project to compare the diffusion of medical technologies for the treatment of coronary heart disease (CHD) between Portugal and the United States. This is an example of a study attempting to utilize techniques at a patient-specific level. A lot of practice pattern differences are observed between countries.

Ideas for Future Research

- International data from IMS Health on drug development and diffusion could be used to analyze the marketing of different drugs in Spain, Portugal, or France.
- As more cross-national research is conducted it will be possible to aggregate the results. There are EU groups that are trying to align the data and look at variations both across and within regions.
- It would be interesting to study the diffusion of a product in low-income countries. It is important to understand why some innovations do not diffuse. They may not be adaptable for some reason. Studies such as this could inform U.S. innovation too in what types of devices are adaptable in what kind of ways. There are many technologies that cannot be used in some countries. It would be beneficial to be able to develop a database of common markers or barriers.

There is an announcement from the National Science Foundation that invites grant applications to create international data sources. EU countries were a particular interest as was the field of social science.

From Evidence to Practice: Improving the Quality and Outcomes of Care

Arlene Bierman, Agency for Healthcare Research and Quality

The AHRQ and its funded centers might offer opportunities for researchers conducting research in the field of technology diffusion. AHRQ's mission is to produce evidence to make health care safer, higher quality, and more accessible, equitable, and affordable. AHRQ works with other offices in the U.S. Department of Health and Human Services and other partners to ensure that the evidence is understood and used. To pursue this mission, AHRQ invests in research and evidence building, creates training materials, and generates measures and data to track and evaluate progress of the U.S. health care system.

AHRQ funds several centers and projects to meet these goals. Examples include:

- The Center for Delivery, Organization, and Markets (CDOM): Provides a locus of leadership and expertise for advances in health care delivery, organization, and markets through research.
- Comparative Health System Performance Initiative Purpose: Identifies, classifies, and compares health care delivery systems and works to accelerate the dissemination and implementation of patient-centered outcomes research evidence.

- Accelerating Change and Transformation in Organizations and Networks (ACTION) III: Develops and tests innovations designed to improve care delivery and disseminates and implements successful interventions and care delivery models in diverse care settings.
- Healthcare Cost and Utilization Project (HCUP): The largest collection of all-payer, encounter-level hospital care data in the United States.
- Center for Evidence and Practice Improvement (CEPI): Generates new knowledge, synthesizes evidence, translates science on what works in health and health care delivery, and catalyzes practice improvement across health care settings.

Some of AHRQs centers focus on synthesizing evidence for dissemination and implementation. Examples include the Evidence-based Practice Center Program, which conducts systematic reviews of comparative effectiveness research, and the AHRQ Healthcare Horizon Scanning Program, which identifies novel interventions that address unmet needs related to AHRQ's priority conditions. The Healthcare Horizon Scanning Program also included a cost analysis pilot project. AHRQ published a Request for Information in February 2016 to solicit input on the feasibility of expanding future possibilities for the Healthcare Horizon Scanning Program.

Language in the Patient Protection and Affordable Care Act requires AHRQ, in consultation with NIH, to broadly disseminate research findings published by the Patient-Centered Outcomes Research Institute (PCORI) and other government supported research relevant to comparative clinical effectiveness research. PCORI is beginning to produce evidence about the effectiveness of different health care delivery systems, which has the potential to impact the technology diffusion. Effective innovations that are currently underutilized will be reviewed as will questions concerning implementation and de-implementation.

Evidence Now is a current AHRQ-funded network focused on improving the delivery of heart health care at more than 1,500 primary care practices across the country. While the primary goal of the intervention is to improve quality of care, a secondary goal is to understand the types of supports that help primary care practices achieve these improved health outcomes.

Physicians – Networks and Characteristics

Competition and Peer-Effects in Medical Technology Diffusion: Evidence from Drug-Eluting Coronary Stents

Pinar Karaca-Mandic, University of Minnesota

Medical technology has been a key driver over the past 50 years in the improvement of life expectancy and quality of life as well as in the increase in health care costs. Previous research about medical technologies focused on its distribution and use. There are large variations in the timing, intensity, and appropriateness of medical technology across regions, hospitals, physicians, and patients. Medical technologies have the potential to be both over- and under-used, which can have health consequences at the population level. Current research on medical technology focuses on treatment variation by hospital and across geographic regions.

Karaca-Mandic is examining how physician interactions through competition and peer effects affect patterns of medical technology diffusion. One current study is focusing on DES diffusion in the Medicare population from April 2003 to December 2004.[11] DES were considered a breakthrough when introduced in 2003. The first DES appeared on the market in 2003 and diffused rapidly. The study found rapid diffusion between April 2003 and March 2004 and a steady state of use thereafter. There was substantial variation in use across cardiologists and hospitals. Faster diffusion was found in markets where cardiology practices faced more competition. There was no evidence that the structure of the hospital market was associated with diffusion.

Another ongoing study is examining spillover effects in provider behavior. Peer effects exist because individuals share information and experiences with colleagues on the products they use. Adoption decisions may be influenced by peer information and actions concerning the new technology. Preliminary results indicate that there is empirical support for peer effects in the diffusion of DES. Future work will attempt to identify the nature of peer effects including conformity or the maintenance of reputation as well as asymmetric peer effects.

The Local Influence of Pioneer Investigators on Technology Adoption: Evidence from New Cancer Drugs

Leila Agha, Boston University and the National Bureau of Economic Research

Agha's current work investigates whether local networks influence medical technology diffusion. The study examines whether physician investigators involved in clinical trials created a geographic spillover for cancer drug diffusion, inducing nearby physicians to adopt more rapidly. She used Medicare claims data from 1998 to 2008 on 21 new cancer drugs and a difference-in-differences model to compare drug adoption in the investigator's region relative to the drug's adoption in other regions and adoption of a control drug in the same region.

Analyses suggest that patients treated in the region where an investigator is leading a pivotal clinical trial are 35 percent more likely to receive the new drug relative to other regions, but this difference disappears by the fourth year after FDA approval for the drug. Follow up conversations with oncologists about why there might be friction in early diffusion suggest that prescribing a new drug can be risky and uncertain because the clinical trial population is generally healthier than the community population and there is uncertainty about dosing.

Preliminary conclusions from this study are that new drug utilization is more intensive in regions within close proximity of the investigator of the pivotal clinical trial. The proximity effect diminishes over time. Patients appear to be more likely to travel to investigator regions; and return to new drug use may be higher in fast-adopting regions.

[11] Karaca-Mandic, P., Town, R. J., & Wilcock, A. (In press). The effect of physician and hospital market structure on medical technology diffusion. *Health Services Research*.

A Study of Variation in ICD Treatment in the United States from a Network Science Perspective

James O'Malley, Dartmouth College

ICDs were FDA-approved in 2006, yet 22.5 percent of patients who receive ICD therapy do not meet clinical guidelines. O'Malley and colleagues are using social network analysis to study variation in and diffusion of ICD therapy use. Specifically, they are trying to determine whether a physician's role in patient care (his or her position in the network) versus the hospital at which care occurs (the structure of the network) matters more.

Hospital networks were summarized using statistical network science and models of social networks, including measures of network density, network centralization, network clustering and centrality, and physician ties within a hospital. These analyses yielded many summary measures at multiple levels. For example, more centralized HRRs have a greater per capita utilization of ICDs. Guideline consistency can be performed at the patient level. Characteristics of network and provider can be analyzed. HRRs with a greater proportion of edges between physicians have a higher proportion of guidelines being met. It is possible that there are more second opinions being discussed about whether ICD is appropriate. Within the network there are mini networks that may be less cognizant of guidelines.

Preliminary results have led to several conclusions and ideas for future directions. Different network measures are related to total utilization and evidence-based utilization of ICD therapy. There are implications for dissemination of new practices or technologies in a health care delivery system. Centralized physician networks may have more efficient adoption of new technology. Network density may be related to reinforcement of guidelines or increased opportunity for peer effects. Future work will focus on the characterization of early ICD adopters with Doximity data and modeling physician peer-to-peer influence with respect to ICD utilization over time.

Discussion: What Resources Does the Field Need?

The projects presented involve multiple levels of analyses including hospitals, providers, and patients. CMS data are a valuable resource, yet these data are limited. The field is moving beyond CMS claims data towards big data. The IMS Health files, for example, can be used to characterize organizational structures in a dynamic way. Obtaining commercial data is a challenge for independent investigators who are not connected to a large institutional infrastructure because of the associated costs. Making these type of data more widely available would benefit the research field immensely.

The richness of data sources has been reduced. Basic information such as state identifiers has been pulled back from many datasets including those from CMS and NCHS. The SEER-Medicare data contains information on FFS beneficiaries yet that portion of the population is decreasing. In the future these data sources will be less generalizable. Merging data on FFS beneficiaries with other datasets would benefit researchers. The SEER-MHOS resource has data on Medicare Advantage beneficiaries, but there is no link between this and the SEER-Medicare database.

There are big startup costs for using Optum, HCCI, and CMS data. NIH-funded investigators are repeatedly paying to obtain these data. Participants advocated for a different arrangement wherein the funder could negotiate an overall agreement with the data sources and then grant access to funded investigators. An NIH- or IC-wide agreement would facilitate wider access to the data.

Collaborating with non-governmental agencies such as pharmaceutical companies, or Google Health, might be a future next step. It is likely that pharmaceutical companies, for example, are asking similar questions and gathering data on the diffusion of their drugs because they have an interest in knowing why it takes a particular drug more time to infiltrate the market. Statisticians working in marketing departments must be looking at similar things. It might be helpful to get a conversation started with some experts at pharmaceutical companies. They probably have tracked the sales of Lipitor, for example, and this is information that is no longer needed.

Collaborating with other NIH initiatives also may be a future next step. NIH's BD2K initiative, or the NIH Health Care Systems Research Collaboratory might be resourceful. BD2K is in the process of creating a discovery index to facilitate data use and the NIH Collaboratory is bringing together researchers that use electronic health data. Hypotheses within different health care systems or within health insurance systems that could move the field forward on a broader scale could be tested.

An open source website is a potential tool for investigators studying diffusion of medical technology to share data and code.

Following the workshop, NIH staff and Principal Investigators of the Health Economics-funded cooperative agreements discussed concrete ways to contribute collectively to the field.

Appendix 1: Agenda

Thursday, May 5, 2016		
9:00 a.m.	Welcome and Introductions Purpose of the Meeting	Jonathan Skinner John Haaga
	HEALTH ECONOMICS PROGRAM COOPERATIVE AGREEMENTS	
9:15	Technology diffusion pathways	Haiden Huskamp Sharon-Lise Normand
9:45	How do patents affect research investments?	Heidi Williams
10:15	Technology diffusion, health outcomes, and expenditures	Jonathan Skinner
10:45	**BREAK**	
	DIFFUSION CASE STUDIES	
11:00	Factors associated with adoption—or abandonment—of surgical procedures	Philip Goodney
11:20	Opioid prescriptions	Ellen Meara
11:40	Choice of treatment for prostate cancer	Bruce Jacobs
12:00 p.m.	Q&A and Discussion	
12:15	**LUNCH**	
1:15	Dissemination and implementation research at the NIH	David Chambers
1:45	**Discussion**: Do diffusion studies explain disparities?	Moderator: John Haaga

INNOVATION

2:15	Regulating innovation with uncertain quality	Robert Town
2:35	Innovation in science	Jay Bhattacharya
2:55	Dormant therapies: Gaps in patent protection available for new drugs	Benjamin Roin
3:15	Q&A and Discussion	
3:30	**BREAK**	
3:45	CMS coverage decision process	Joseph Chin
4:05	**Discussion**: What can we learn from cross-national comparisons?	Moderator: Jonathan Skinner
4:45	**ADJOURN**	

Friday, May 6, 2016

9:00 a.m.	Relevant AHRQ initiatives	Arlene Bierman David Knutson

PHYSICIANS—NETWORKS AND CHARACTERISTICS

9:20	The effect of physician and hospital market structure on medical technology diffusion	Pinar Karaca-Mandic
9:40	The local influence of pioneer investigators on technology adoption: Evidence from new cancer drugs	Leila Agha
10:00	An investigation of evidence-based implantable cardioverter defibrillator treatment in the United States from a social network perspective	James O'Malley
10:20	Q&A and Discussion	
10:35	**Discussion**: What resources does the field need to progress?	Moderator: Jonathan Skinner
11:20	**BREAK**	
11:35	Steering Committee Executive Session	
12:30 p.m.	**ADJOURN**	

Appendix 2: Workshop Participants

Cooperative Agreement Awardees

Haiden Huskamp, Harvard University
Sharon-Lise Normand, Harvard University
Jonathan Skinner, Dartmouth College
Heidi Williams, Massachusetts Institute of Technology

Invited Speakers

Leila Agha, Boston University
Jay Bhattacharya, Stanford University
Arlene Bierman, Agency for Healthcare Research and Quality
David Chambers, National Cancer Institute, NIH
Joseph Chin, Centers for Medicare & Medicaid Services
Philip Goodney, Dartmouth College Hitchcock Medical Center
John Haaga, National Institute on Aging, NIH
Bruce Jacobs, University of Pittsburgh
Pinar Karaca-Mandic, University of Minnesota
Ellen Meara, Dartmouth College
A. James O'Malley, Dartmouth College
Benjamin Roin, Massachusetts Institute of Technology
Robert Town, University of Pennsylvania

NIH and Contractor Staff

Partha Bhattacharyya, National Institute on Aging
Gregory Bloss, National Institute on Alcohol Abuse and Alcoholism
Rachel Britt, Office of the Director
Leslie Derr, Office of the Director
Nicole Devieux, Rose Li and Associates, Inc.
Sarah Q. Duffy, National Institute on Drug Abuse
Anneliese Ebersole, Rose Li and Associates, Inc.
Chandra Keller-Allen, Rose Li and Associates, Inc.
Rose Maria Li, Rose Li and Associates, Inc.
Hiromi Ono, National Institute on Drug Abuse
Agnes Rupp, National Institute of Mental Health
Elizabeth Wilder, Office of the Director

Other

Stefani Schmidt, MITRE Corporation